Remarks

Rejection of Claims 23 and 26 Under 35 U.S.C. § 102(b)

Claims 23 and 26 stand rejected as anticipated by Porter (*J. Histochem. Cytochem., 43:*791-800, 1995). This rejection is respectfully traversed.

The claims are directed to a method by which tumor endothelial cells are identified using a specific-binding antibody to osteonectin. A population of tumor cells containing endothelial cells is contacted with the antibody, and cells which bind to the antibody are detected. The cells which are bound are identified as tumor endothelial cells.

Porter is cited as teaching the use of a monoclonal antibody to SPARC to stain tumor tissues including renal cell carcinoma, lung adenocarcinoma, breast adenocarcinoma, giant-cell tumor of bone, astrocytes in low grade glioma, and endometrial adenocarcinoma. The U.S. Patent and Trademark Office does not explain how all the elements of the claim are met by these teachings.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California,* 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish

the inherency of that result or characteristic. *In re Rijckaert,* 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993). To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' *In re Robertson,* 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999). See M.P.E.P. § 2112.

Porter does not teach the presence in its tissue samples of endothelial cells. In order for Porter to anticipate the method of claims 23 and 26, the tissue samples would necessarily need to contain endothelial cells.

The U.S. Patent and Trademark Office points to Figures 5 and 6 of Porter. Figure 5 shows human tumors stained with antibody. There is no teaching that the staining seen in Figure 5 is in endothelial cells rather than in the carcinoma cells themselves. Figure 6 shows staining in two breast cancers. Porter points out that the staining is in the malignant cells *per se* (arrows) and absent from the benign duct and lobular epithelium (arrowheads). Neither of these figures demonstrates the staining and identification of endothelial cells.

No extrinsic evidence has been supplied to demonstrate that endothelial cells would necessarily be present in Porter's tissue samples. The mere fact that endothelial cells might

possibly be present is not sufficient to meet the legal standard for anticipation by inherency. Thus Porter does not teach the first step (contacting) of the claimed method. Porter also does not teach the third step (identifying).

Withdrawal of the rejection is respectfully requested because Porter does not teach the claimed method, either explicitly or inherently.

Rejection of Claims 23, 24, 26, and 27 Under 35 U.S.C. § 103

Claims 23, 24, 26, and 27 stand rejected as unpatentable over the combination of Porter (discussed above) in view of Long (US 20040214241) and Taniguchi (Int. J. Cancer 86:799-805, 2000).

Porter is cited as using anti-SPARC antibodies to immunostain cancer cells. Long is cited as teaching the use of anti-osteonectin antibodies to isolate bone precursor cells from bone marrow, bone, or blood. Taniguchi is cited as teaching that tumor endothelial cells are a new target for cancer therapy. The U.S. Patent and Trademark Office concludes that one of skill in the art would have been motivated by Taniguchi to isolate tumor endothelial cells so that new anti-cancer therapies could be tested upon them. It asserts that doing so from a population of tumor cells in a tissue or a population of tumor cells in a body fluid would have been obvious based on Long's teaching of isolation of bone precursor cells (different cell type) from normal

bone marrow, normal bone, or normal blood (different cell populations). And it asserts that one of skill in the art would have known that one could identify and obtain endothelial cells from a population of tumor cells based on Porter.

However, while Long teaches the isolation of bone precursor cells from normal issue and body fluid, it does not teach or suggest anything at all about tumor endothelial cells or using tumor cells as a population from which to identify endothelial cells. Certainly one of skill in the art who wanted to obtain bone precursor cells would not turn to a population of tumor cells for a source. One of skill in the art would not knowingly choose a malignant cell source for uses as taught by Long, such as treatment of certain bone related disorders and diseases, such as osteoporosis or fracture repair. Thus the combination of Long's teaching with Porter's would not have been made. Their goals are antithetical and would prevent the combination of teachings.

Moreover, as discussed above, Porter does not teach the differential expression of osteonectin in endothelial cells relative to tumor cells. Without such a teaching, one of skill in the art would not have known that one could identify endothelial cells within a population of tumor cells using anti-osteonectin antibodies. On the contrary, Porter provides a teaching away from such a method by teaching that cancer cells themselves express osteonectin (see Figures 5 and 6). Given Porter's teaching, one of skill in the art would not have been motivated to isolate endothelial cells from a population of tumor cells using an anti-osteonectin antibody. Based on

Porter's teachings, one of skill in the art would not have had a reasonable expectation that such a method would be successful. Based on Porter's teachings, one would have expected to identify tumor cells *per se* with such an antibody. Thus the three references asserted do not present a *prima facie* case of obviousness.

Withdrawal of this rejection is respectfully requested.

A speedy allowance of all claims is requested.

Respectfully submitted,

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